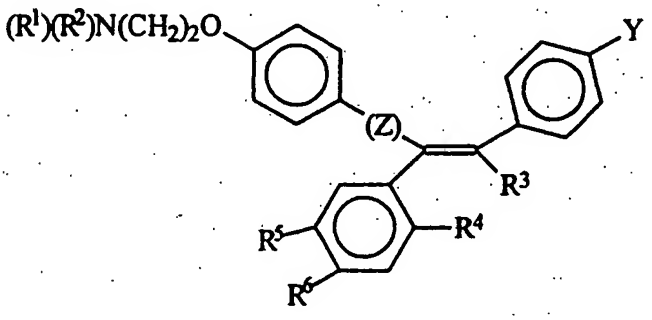
WHAT IS CLAIMED IS:

1. A therapeutic method for treating a condition selected from the group consisting of atherosclerosis, thrombosis, myocardial infarction and stroke, comprising administering to a mammal afflicted with said condition, an effective amount of a compound of formula (I):

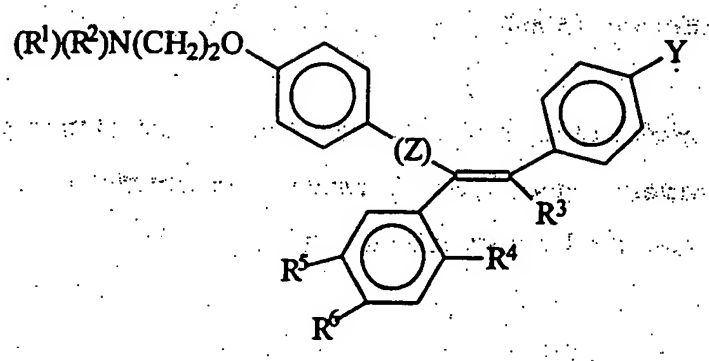


(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

2. A method comprising administering to a mammal at risk of a cardiovascular condition the following:

an effective amount of a compound of formula (I)



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof, wherein the amount is administered over time to the mammal to prevent a cardiovascular condition selected from the group consisting of thrombosis, myocardial infarction, and stroke.

3. The method of claim 1 or 2 wherein Z is a covalent bond and Y is H.

4. The method of claim 3 wherein R^3 is 2-chloroethyl.

5. The method of claim 3 wherein R^1 and R^2 are methyl.

6. The method of claim 4 wherein R^1 and R^2 are methyl.

7. The method of claim 3 wherein R^5 is I and R^4 and R^6 are H.

8. The method of claim 3 wherein R^6 is I and R^4 and R^5 are H.

9. The method of claim 1 or 2 wherein R^4, R^5 and R^6 are H.

10. The method of claim 1 or 2 wherein the compound of formula (I) is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

11. The method of claim 1 or 2 wherein the compound of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

12. The method of claim 1 or 2 wherein the compound of formula (I) is toremifene or a pharmaceutically acceptable salt thereof.

13. The method of claim 1 wherein the compound of formula (I) significantly reduces the rate of completion of the cell cycle and division of vascular smooth muscle cells.

14. The method of claim 1 wherein the compound of formula (I) does not form cellular DNA adducts.

15. The method of claim 1 wherein the condition is atherosclerosis.

16. The method of claim 1 wherein the compound of formula (I) is administered locally to an arterial lesion associated with atherosclerosis.

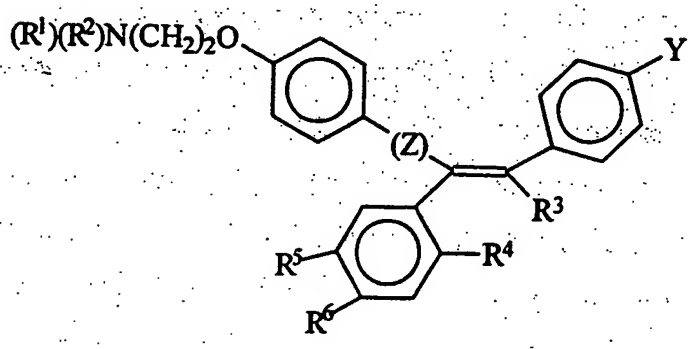
17. The method of claim 1 wherein the compound of formula (I) is administered in a sustained release dosage form.

18. The method of claim 1 wherein the administration is systemic.

19. The method of claim 1 wherein the administration is oral.

20. The method of claim 1 or 2 wherein the administration is in a series of doses.

21. A therapeutic method for treating atherosclerosis, comprising systemically administering to a mammal afflicted with atherosclerosis, an effective amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

22. The method of claim 21 wherein the compound of formula (I) acts to inhibit pathological activity of vascular smooth muscle cells, to inhibit lipid accumulation by vessels, to decrease the development of a lesion associated with said atherosclerosis, to inhibit the formation of a lesion associated with said atherosclerosis, to increase plaque stability in a lesion associated with said atherosclerosis, or any combination thereof.

23. The method of claim 21 wherein the compound of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

24. The method of claim 1, 2 or 21 wherein the compound indirectly or directly increases the level of active TGF-beta.

25. A method for identifying an agent which increases the level of TGF-beta in a human comprising:

(a) contacting cultured explant human aortic smooth muscle cells (hVSMC) with said agent in an amount effective to reduce or inhibit the rate of proliferation of said cells;

(b) contacting said hVSMC resulting from step (a) with a moiety which specifically binds to TGF-beta in an amount effective to block the binding of TGF-beta to the TGF-beta receptors of said hVSMC and determining the rate of proliferation; and

(c) determining whether the rate of proliferation of said hVSMC resulting from step (b) is increased relative to the rate of proliferation of the hVSMC which are contacted with said agent in step (a).

26. The method of claim 25 wherein the moiety which binds TGF-beta is a polyclonal antibody.

27. The method of claim 25 wherein the moiety which binds TGF-beta is a monoclonal antibody.

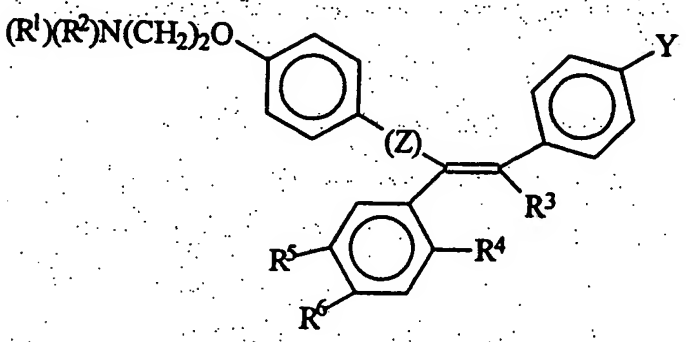
28. The method of claim 25 wherein the agent is a TGF-beta production stimulator.

29. The method of claim 25 wherein the agent is a TGF-beta activator.

30. The method of claim 25 wherein the agent increases the production of TGF-beta mRNA in said hVSMC.

31. The method of claim 25 wherein the agent increases the cleavage of the latent form of TGF-beta produced by said hVSMC.

32. A kit comprising, separately packaged, a catheter adapted for the local delivery of a therapeutic agent to a site in the lumen of a mammalian vessel and a unit dosage of a therapeutic agent of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof, wherein the unit dosage is effective to inhibit pathological activity of the smooth muscle cells at said site.

33. The kit f claim 32 wherein the catheter is adapted to deliver the unit dosage form to an arterial lesion.

34. The kit of claim 32 wherein the catheter is adapted to deliver the unit dosage to a vessel site which has been subjected to coronary angioplasty.

35. The kit of claim 32 wherein the therapeutic agent of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

36. The kit of claim 32 wherein the therapeutic agent of formula (I) is toremifene or a pharmaceutically acceptable salt thereof.

37. The kit of claim 32 wherein the therapeutic agent of formula (I) indirectly or directly increases the level of active TGF-beta.

38. A kit comprising, separately packaged, a catheter adapted for the local delivery of a therapeutic agent to a site in the lumen of a mammalian vessel and a unit dosage of droloxifene and pharmaceutically acceptable salts thereof, wherein the unit dosage is effective to inhibit pathological activity of the smooth muscle cells at said site.

39. A method for determining TGF-beta *in vitro*, thereby identifying a patient at risk for atherosclerosis or monitoring a recipient that has received one or more administrations of a therapeutic agent which increases the level of TGF-beta, which method comprises:

(a) contacting a sample of blood serum or plasma from said patient or said recipient with a capture moiety, to form a capture complex comprising said capture moiety and TGF-beta;

(b) contacting the capture complex with a detection moiety which binds TGF-beta and which comprises a detectable label, or a site which binds a detectable label, to form a detectable complex: and

(c) detecting the presence of the detectable complex, so as to determine the presence of TGF-beta in said sample.

40. A method for determining active TGF-beta *in vitro*, comprising:

(a) contacting a sample of serum or plasma from an individual with a capture moiety which binds TGF-beta, to form a capture complex comprising said capture moiety and TGF-beta;

(b) combining the capture complex with a detection moiety which binds TGF-beta and which has a detectable label, to form a detectable complex, wherein either or both the capture and detection moiety bind active but not latent TGF-beta; and

(c) determining the presence of a detectable label in the detectable complex, so as to determine the presence of active TGF-beta in the sample.

41. The method of claim 39 or 40 wherein the capture moiety is immobilized on a solid substrate.

42. The method of claim 39 or 40 wherein the capture moiety is a solution phase capture moiety.

43. The method of claim 40 wherein the capture moiety and detection moiety are capable of binding both latent and active TGF-beta.

44. The method of claim 39 or 40 wherein the capture moiety is a first anti-TGF-beta antibody and the detection moiety is a second anti-TGF-beta antibody.

45. The method of claim 39 wherein the capture moiety or the detection moiety recognizes active TGF-beta only.

46. The method of claim 39 or 40 wherein the capture moiety is TGF-beta type II receptor extracellular domain and the detection moiety is an anti-TGF-beta antibody.

47. The method of claim 39 or 40 wherein the presence of the detectable complex is detected by reacting the detectable complex with an antibody comprising a detectable label, which binds to said detectable complex, and determining the presence of the label.

48. The method of claim 39 wherein the therapeutic agent is a TGF-beta production stimulator.

49. The method of claim 39 wherein the therapeutic agent is a TGF-beta activator.

50. The method of claim 39 or 40 wherein the capture or the detection moiety is TGF-beta type II extracellular domain.

51. The method of claim 50 wherein the TGF-beta type II extracellular domain has a methionine residue at position 5.

52. The method of claim 39 or 40 wherein the detection moiety is an anti-TGF-beta antibody.

53. The method of claim 39 or 40 wherein the capture moiety is an anti-TGF-beta antibody.

54. The method of claim 40 wherein the moiety that binds active but not latent TGF-beta is TGF-beta type II receptor extracellular domain.

55. The method of claim 54 wherein the TGF-beta type II receptor extracellular domain has a methionine residue at position 5.

56. A test kit for determining TGF-beta *in vitro* comprising packaging material enclosing, separately packaged, (a) a capture moiety capable of binding TGF-beta, and (b) a detection moiety capable of binding to TGF-

beta, which moiety comprises a detectable label or a binding site for a detectable label.

57. The test kit of claim 56 wherein said capture moiety is immobilized on a solid substrate.

58. The test kit of claim 56 wherein said capture moiety is present in solution.

59. The test kit of claim 56 wherein the capture moiety is a first anti-TGF-beta antibody.

60. The test kit of claim 56 wherein the detection moiety is a second anti-TGF-beta antibody.

61. The test kit of claim 56 wherein the capture moiety is TGF-beta type II receptor extracellular domain.

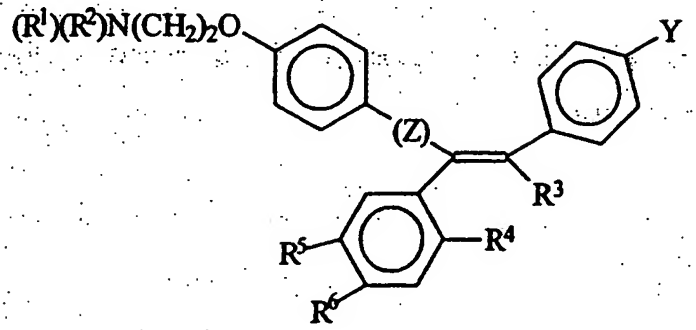
62. The test kit of claim 61 wherein the TGF-beta type II receptor extracellular domain is derived from a bacterial expression system.

63. The test kit of claim 56 wherein the detection moiety is an anti-TGF-beta antibody.

64. The test kit of claim 60 or 63 further comprising, separately packaged, an antibody which binds to said detection moiety, which comprises a detectable label.

65. A therapeutic method comprising inhibiting smooth muscle cell (SMC) proliferation associated with procedural vascular trauma comprising the administration to a mammal subjected to said procedure, an effective

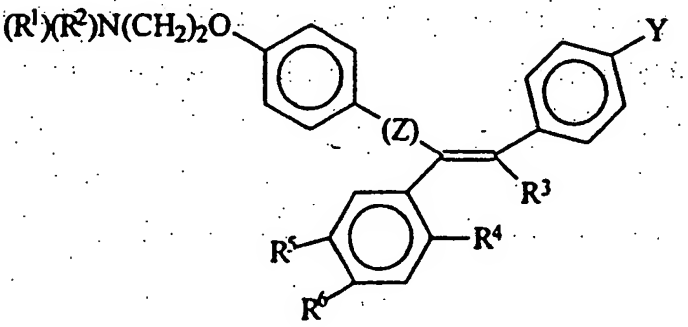
cytostatic SMC proliferation inhibitory amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

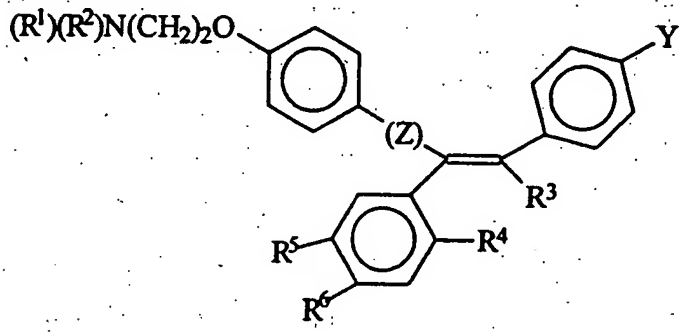
66. A therapeutic method comprising inhibiting vascular smooth muscle cell proliferation associated with procedural vascular trauma comprising administration to a mammal subjected to said procedural trauma an effective antiproliferative amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

67. A therapeutic method comprising inhibiting non-aortal vascular smooth muscle cell proliferation associated with procedural vascular trauma comprising administering to a mammal, such as a human, subjected to said procedural vascular trauma an effective cytostatic antiproliferative amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H or together with R^3 is -CH_2-CH_2- or -S-, R^5 is I, OH, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H; or a pharmaceutically acceptable salt thereof.

68. The method of claim 65 wherein the procedural vascular trauma is due to organ transplantation, vascular surgery, transcatheter vascular therapy,

vascular grafting, placement of a vascular shunt or placement of an intravascular stent.

69. The method of claim 67 wherein the compound of formula (I) is tamoxifen or a pharmaceutically acceptable salt thereof.

70. The method of claim 65 or 66 wherein the compound of formula (I) is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

71. The method of claim 65, 66 or 67 wherein the compound of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

72. The method of claim 21, 65, 66 or 67 wherein the compound of formula (I) is toremifene or a pharmaceutically acceptable salt thereof.

73. The method of claim 65, 66 or 67 wherein the administration is to a human patient.

74. The method of claim 65, 66 or 67 wherein the administration is before, during or after said procedure.

75. The method of claim 65, 66 or 67 wherein the administration is in a series of spaced doses.

76. The method of claim 65, 66 or 67 wherein the administration is parenteral.

77. The method of claim 65, 66 or 67 wherein the administration is oral.

78. The method of claim 65, 66 or 67 wherein the administration is systemic.

79. The method of claim 65, 66 or 67 wherein the compound of formula (I) is administered via a sustained release dosage form.

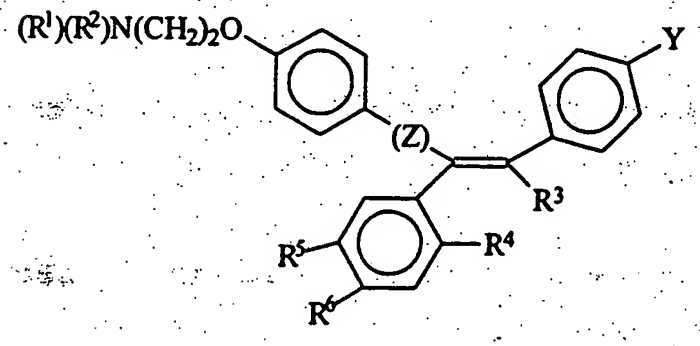
80. The method of claim 65, 66 or 67 wherein the administration is localized at the site of the vascular trauma.

81. The method of claim 65, 66 or 67 wherein the compound directly or indirectly increases the level of active TGF-beta.

82. The method of claim 67 wherein the compound of formula (I) is raloxifene, or a pharmaceutically acceptable salt thereof.

83. The method of claim 67 wherein the compound of formula (I) is droloxifene, or a pharmaceutically acceptable salt thereof.

84. A therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter comprising administering to a mammal at risk of or afflicted with said cardiovascular indication, a cytostatic dose of a therapeutic agent, wherein the therapeutic agent is a compound of formula (I):



(I)

wherein Z is C=O r a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated

heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H, R^5 is I, $O(C_1$-$C_4)$alkyl or H and R^6 is I, $O(C_1$-$C_4)$alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

85. The method of claim 84 wherein the cytostatic dose is effective to increase the level of TGF-beta so as to inhibit smooth muscle cell proliferation, inhibit lipid accumulation, increase plaque stability, or any combination thereof.

86. The method of claim 84 wherein the compound of formula (I) is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

87. The method of claim 84 wherein the compound of formula (I) is idoxifene or a pharmaceutically acceptable salt thereof.

88. The method of claim 84 wherein the compound of formula (I) is toremifene or a pharmaceutically acceptable salt thereof.

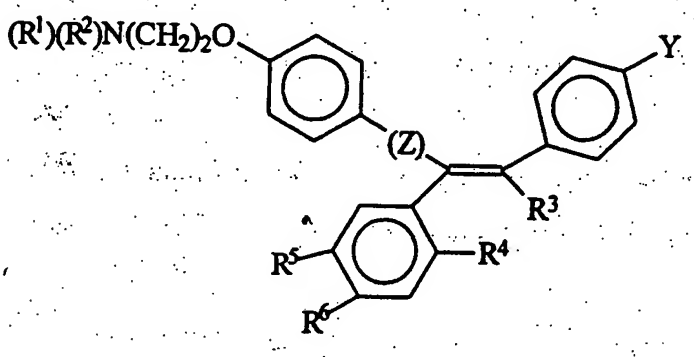
89. The method of claim 84 wherein the administration is systemic.

90. The method of claim 84 wherein the compound of formula (I) is administered via a sustained release dosage form.

91. The method of claim 84 wherein the administration is localized at the site of the vascular trauma.

92. The method of claim 84 wherein the compound directly or indirectly increases the level of active TGF-beta.

93. A therapeutic method of increasing the level of TGF-beta in a mammal in need thereof, comprising administering an effective amount of a compound of formula (I):



(I)

wherein Z is C=O or a covalent bond; Y is H or O(C_1-C_4)alkyl, R^1 and R^2 are individually (C_1-C_4)alkyl or together with N are a saturated heterocyclic group, R^3 is ethyl or chloroethyl, R^4 is H or together with R^3 is -CH_2-CH_2- or -S-, R^5 is I, OH, O(C_1-C_4)alkyl or H and R^6 is I, O(C_1-C_4)alkyl or H with the proviso that when R^4, R^5, and R^6 are H, R^3 is not ethyl; or a pharmaceutically acceptable salt thereof.

94. A method of treating diabetics at risk of, or afflicted with, vascular disease, comprising: administering an amount of tamoxifen or a structural analog thereof effective to indirectly or directly increase the level of active TGF-beta in said diabetic.

95. The method of claim 94 wherein the structural analog of tamoxifen is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, raloxifene, droloxifene, toremifene, or a pharmaceutically acceptable salt thereof.

96. The method of claim 94 wherein the structural analog of tamoxifen is idoxifene, 4-iodotamoxifen, 3-iodotamoxifen, toremifene, or a pharmaceutically acceptable salt thereof.

97. The method of claim 94 wherein the structural analog of tamoxifen is idoxifene, or a pharmaceutically acceptable salt thereof.

98. The method of claim 94 wherein the structural analog of tamoxifen is toremifene, or a pharmaceutically acceptable salt thereof.

99. The method of claim 93 or 94 wherein the increase in TGF-beta reduces or inhibits diabetic retinopathy.

100. The method of claim 93 wherein the mammal is diabetic.

101. The method of claim 100 wherein the diabetic has retinopathy.

102. The method of claim 93 wherein the compound indirectly or directly increases the level of active TGF-beta in vascular tissue.

103. The method of claim 1, 2, 21 or 93 wherein the compound is a TGF-beta production stimulator.

104. The method of claim 1, 2, 21 or 93 wherein the compound is a TGF-beta activator.

105. The method of claim 1, 2, 21 or 93 wherein the compound increases the production of TGF-beta mRNA.

106. The method of claim 1, 2, 21 or 93 wherein the compound increases the cleavage of the latent form of TGF-beta.

107. The method of claim 1, 2, 21 or 93 wherein the compound increases the bioavailability of TGF-beta.

108. The method of claim 93 wherein the compound is idoxifene or a pharmaceutically acceptable salt thereof.

109. The method of claim 93 wherein the compound is toremifene or a pharmaceutically acceptable salt thereof.

110. The method of claim 93 wherein the compound is droloxifene or a pharmaceutically acceptable salt thereof.

111. The method of claim 93 wherein the compound is tamoxifen or a pharmaceutically acceptable salt thereof.

112. The method of claim 1, 2, 21, 65, 66, 67, 84 or 93 wherein the compound forms cellular DNA adducts at level which is reduced relative to DNA adduct formation by tamoxifen.

113. The method of claim 1, 2, 21, 65, 66, 67, 84 or 93 wherein the compound has estrogenic activity which is reduced relative to the estrogenic activity of tamoxifen.

114. The method of claim 21, 65, 66, 67, 84 or 93 wherein the compound does not form cellular DNA adducts.

115. The method of claim 1, 2, 21, 65, 66, 67, 84 or 93 wherein the compound has no estrogenic activity.

116. A method of increasing the level of TGF-beta in a mammal in need thereof, comprising administering an effective amount of an agent that directly or indirectly elevates the level of active TGF-beta in said mammal, wherein the agent has reduced estrogenic activity relative to

tamoxifen, reduced DNA adduct formation relative to tamoxifen, or any combination thereof.

117. The method of claim 116 wherein the agent is a structural analog of tamoxifen or a pharmaceutically acceptable salt thereof.

118. The method of claim 116 wherein the agent is idoxifene or a pharmaceutically acceptable salt thereof.

119. The method of claim 116 wherein the agent is toremifene or a pharmaceutically acceptable salt thereof.

120. The method of claim 67 wherein the non-aortal smooth muscle cells which are inhibited are present in a non-coronary artery.

121. The method of claim 94 wherien the amount is effective to inhibit the proliferation of vascular tissue.